

CLAIMS

- 1 1. A recombinant microorganism that displays on its surface a binding
2 moiety that, when administered to an animal, competes with a ligand for binding to a receptor
3 for the ligand, wherein the binding moiety comprises an oligosaccharide which comprises a
4 sugar residue that is attached to an acceptor moiety by a glycosyltransferase that is encoded
5 by an exogenous nucleic acid which is present in the microorganism.
- 1 2. The recombinant microorganism of claim 1, wherein the microorganism
2 is selected from the group consisting of bacteria, fungi, Mycoplasma, and yeast.
- 1 3. The recombinant microorganism of claim 1, wherein the oligosaccharide
2 further comprises at least a second sugar residue that is attached to an acceptor moiety by at
3 least a second glycosyltransferase.
- 1 4. The recombinant microorganism of claim 3, wherein the second
2 glycosyltransferase is encoded by a second exogenous nucleic acid which is present in the
3 microorganism.
- 1 5. The recombinant microorganism of claim 1, wherein the receptor is
2 present on a surface of a cell.
- 1 6. The recombinant microorganism of claim 5, wherein the cell is an
2 epithelial or endothelial cell that comprises a mucosal membrane of an animal.
- 1 7. The recombinant microorganism of claim 1, wherein the binding moiety
2 is a mimic of a receptor for a toxin or adhesin of a pathogenic organism.
- 1 8. The recombinant microorganism of claim 7, wherein the toxin is an
2 enterotoxin.

1 9. The recombinant microorganism of claim 7, wherein the toxin is selected
2 from the group consisting of shiga toxins, clostridial toxins, cholera toxins, *E. coli*
3 enterotoxins, and Staphylococcal enterotoxins.

1 10. The recombinant microorganism of claim 9, wherein the toxin is a shiga
2 toxin.

1 11. The recombinant microorganism of claim 10, wherein the shiga toxin is
2 selected from the group consisting of, Stx, Stx1, Stx2, Stx2c, Stx2d, and Stx2e.

1 12. The recombinant microorganism of claim 11, wherein the microorganism
2 displays on its surface a mimic for all of the receptors in the group consisting of Stx1, Stx2,
3 Stx2c and Stx2d.

1 13. The recombinant microorganism of claim 9, wherein the toxin is a
2 clostridial toxin.

1 14. The recombinant microorganism of claim 13, wherein the clostridial
2 toxin is selected from the group consisting of tetanus toxin, botulinum toxin, and *C. difficile*
3 toxins A and B.

1 15. The recombinant microorganism of claim 9, wherein the toxin is selected
2 from the group consisting of cholera toxin, *E. coli* heat labile enterotoxin types I and II, and
3 ST toxins.

1 16. The recombinant microorganism of claim 7, wherein the binding moiety
2 is a mimic of an adhesin receptor.

1 17. The recombinant microorganism of claim 16, wherein the adhesin is a
2 CFA adhesin of an enterotoxigenic *E. coli*.

1 18. The recombinant microorganism of claim 17, wherein the binding moiety
2 is a mimic of a receptor for *E. coli* CS3 pili.

1 19. The recombinant microorganism of claim 17, wherein the binding moiety
2 is a mimic of a receptor for K88ad fimbriae.

1 20. The recombinant microorganism of claim 16, wherein the binding moiety
2 is a mimic of a receptor for an adhesin of *Entamoeba histolyticum*.

1 21. The recombinant microorganism of claim 16, wherein the binding moiety
2 is a mimic of a receptor for an adhesin of a virus.

1 22. The recombinant microorganism of claim 21, wherein the virus is a
2 rotavirus.

1 23. The recombinant microorganism of claim 22, wherein the rotavirus is a
2 porcine rotavirus.

1 24. The recombinant microorganism of claim 1, wherein the binding moiety
2 is a mimic of a receptor for a virus.

1 25. The recombinant microorganism of claim 1, wherein the binding moiety
2 competes with a pathogenic organism for binding to a corresponding receptor on an animal
3 epithelial or endothelial cell.

1 26. The recombinant microorganism of claim 25, wherein the
2 oligosaccharide comprises a terminal sialic acid or galactose residue.

1 27. The recombinant microorganism of claim 26, wherein the pathogenic
2 organism is selected from the group consisting of *Staphylococcus pneumonia*, *H. influenza*,
3 *H. parainfluenza*, *Chlamydia trachomatis* and *Pseudomonas spp.*

1 28. The recombinant microorganism of claim 25, wherein the
2 oligosaccharide comprises a terminal mannose residue and the pathogenic organism is
3 *Acanthamoeba*.

1 29. The recombinant microorganism of claim 25, wherein the
2 oligosaccharide comprises a terminal fucose residue.

1 30. The recombinant microorganism of claim 29, wherein the
2 oligosaccharide comprises a Fuc α 1,2-Gal moiety and the pathogenic organism is *Candida*
3 *albicans*.

1 31. The recombinant microorganism of claim 29, wherein the
2 oligosaccharide comprises a 2'-Fuc or a 3'-Fuc linkage.

1 32. The recombinant microorganism of claim 31, wherein the pathogenic
2 organism is *Helicobacter pylori*.

1 33. The recombinant microorganism of claim 1, wherein the binding moiety
2 is a mimic of a receptor for a cell involved in inflammation.

1 34. The recombinant microorganism of claim 33, wherein the
2 oligosaccharide comprises a 3'-sialoside or a 6'-sialoside.

1 35. The recombinant microorganism of claim 33, wherein the
2 oligosaccharide comprises sialyl Lewis^x or sialyl Lewis^a.

1 36. The recombinant microorganism of claim 1, wherein the animal is
2 selected from humans, pigs, cows, horses, canines, felines, chickens, turkeys, goats, rabbits,
3 sheep, geese, ducks.

1 37. The recombinant microorganism of claim 1, wherein the binding moiety
2 comprises an oligosaccharide selected from the group consisting of:

NeuNAc α [2 \rightarrow 3]

41. The recombinant microorganism of claim 37, wherein the binding moiety comprises NeuNAc.

1 **49.** The recombinant microorganism of claim 46, wherein the enzyme is
2 involved in synthesis of a nucleotide that comprises the nucleotide sugar.

1 **50.** The recombinant microorganism of claim 46, wherein the enzyme is
2 involved in synthesis of a sugar that comprises the nucleotide sugar.

1 **51.** The recombinant microorganism of claim 46, wherein the one or more
2 sugars transferred to the acceptor molecule by the exogenous glycosyltransferases make up
3 the entirety of the receptor mimic.

1 **52.** The recombinant microorganism as in claim 1, wherein a combination of
2 sugars of the acceptor molecule and the one or more sugars transferred to the acceptor
3 molecule by the exogenous transferases make up the entirety of the receptor mimic.

1 **53.** The recombinant microorganism as in claim 1, wherein the completed
2 acceptor molecule has a terminal residue to which the exogenous glycosyltransferases transfer
3 sugars to make up the receptor mimic.

1 **54.** The recombinant microorganism as in claim 1, wherein the acceptor
2 molecule is an incomplete endogenous molecule and at least one of the exogenous
3 glycosyltransferases competes with an endogenous glycosyltransferase to transfer said sugar
4 molecule thereto.

1 **55.** The recombinant microorganism as in claim 1, wherein the binding
2 moiety is anchored to the outer surface of the microorganism.

1 **56.** The recombinant microorganism as in claim 55, wherein the
2 microorganism is gram negative and the acceptor molecule is a lipopolysaccharide.

1 **57.** The recombinant microorganism as in claim 56, wherein the acceptor
2 molecule is all or a portion of the core of the lipopolysaccharide.

sub A3
1 58. The recombinant microorganism as in claim 1, wherein said
2 microorganism is selected from a genus selected from the group consisting of *Escherichia*,
3 *Salmonella*, *Acidophilus*, *Lactobacillus*, *Lactococcus* and *Bifidobacterium*.

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1 59. The recombinant microorganism as in claim 58, wherein said
2 microorganism is selected from a species selected from the group consisting of *Escherichia*
3 *coli* and *Salmonella enterica* sv typhimurium.

1 60. The recombinant microorganism as in claim 1, wherein the
2 microorganism is chosen by reason of having reduced production of external masking
3 polysaccharide molecules other than said acceptor molecule to enhance exposure of the
4 receptor mimic.

1 61. The recombinant microorganism as in claim 60, wherein the
2 microorganism has reduced production of external molecules selected from the group
3 comprising a slime layer, capsule or exopolysaccharide.

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1 62. The recombinant microorganism as in claim 1, wherein the
2 microorganism is selected to provide some resistance to antimicrobial activity of microflora
3 potentially resident in the gut.

1 63. The recombinant microorganism as in claim 1, wherein the
2 microorganism is resistant to the major families of colicins.

1 64. The recombinant microorganism as in claim 1, wherein all or some of the
2 one or more glycosyl transferases are naturally occurring.

1 65. The recombinant microorganism as in claim 1, wherein genes encoding
2 all or some of the one or more glycosyl transferases are modified to stabilise phase variation.

1 66. A recombinant microorganism expressing one or more exogenous sugar
2 transferases, or one or more exogenous nucleotide sugar precursor synthesising enzymes, said

3 microorganism also expressing an acceptor molecule, said one or more exogenous sugar
4 transferases being specific for the transfer of one or more sugar residues represented
5 progressively from a non reducing terminal end of a receptor of either a toxin or an adhesin of
6 a pathogenic organism, the exogenous sugar transferases progressively transferring said one
7 or more sugar residues onto the acceptor molecule to thereby form a chimeric carbohydrate
8 molecule with an exposed receptor mimic, said sugar precursor enzymes forming nucleotide
9 precursors that are transferred to said acceptor molecule to make up said chimeric
10 carbohydrate, said exposed receptor mimic capable of binding the toxin or the adhesin.

1 67. A pharmaceutical preparation for administration to a mucosal surface,
2 said preparation including a delivery microorganism or a partially or fully purified non-toxic
3 preparation of a carbohydrate molecule therefrom, at least a part of said carbohydrate
4 molecule acting as an exposed receptor mimic, said receptor mimic capable of binding a toxin
5 or an adhesin of a pathogen that normally binds to said mucosal surface, said pharmaceutical
6 preparation being carried in a pharmaceutically acceptable excipient.

1 68. The pharmaceutical preparation as in claim 67, wherein the delivery
2 microorganism is a recombinant microorganism expressing one or more exogenous sugar
3 transferases and an acceptor molecule, said one or more exogenous sugar transferases being
4 specific for transfer of one or more sugar residues represented progressively from a non
5 reducing terminal end of a receptor of either a toxin or an adhesin of a pathogenic organism,
6 said delivery microorganism expressing an acceptor molecule, and progressively transferring
7 said one or more sugar residues onto the acceptor molecule to thereby form the chimeric
8 carbohydrate molecule with the receptor mimic, said exposed receptor mimic capable of
9 binding the toxin or the adhesin.

1 69. The pharmaceutical preparation as in claim 67, wherein the receptor
2 mimic is a mimic of the receptor of a toxin.

1 70. The pharmaceutical preparation as in claim 69, wherein the toxin is
2 selected from the group consisting of shiga toxins, clostridial toxins, cholera toxins, *E. coli*
3 enterotoxins, and Staphylococcal enterotoxins.

1 71. The pharmaceutical preparation as in claim 70, wherein the toxin is a
2 shiga toxin.

1 72. The pharmaceutical preparation as in claim 70, wherein the toxin is a
2 clostridial toxin.

1 73. The pharmaceutical preparation as in claim 67, wherein the receptor
2 mimic is partially or wholly formed within a sugar moiety of selected from the group
3 comprising:

4 Gal α [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,
5 Gal α [1 \rightarrow 4]Gal β ,
6 GalNAc β [1 \rightarrow 3]Gal α [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,
7 Gal β [1 \rightarrow 4]GlcNAc,
8 Gal α [1 \rightarrow 3]Gal β [1 \rightarrow 4]Glc,
9 Gal α [1 \rightarrow 3]Gal β [1 \rightarrow 4]GlcNAc,
10 Gal β [1 \rightarrow 4]GlcNAc β [1 \rightarrow 3]Gal β [1 \rightarrow 4]Glc,
11 Glc α [1 \rightarrow 6]Glc,
12 Glc α [1 \rightarrow 6]Glc α [1 \rightarrow 6]Glc,
13 NeuNAc,
14 Gal β [1 \rightarrow 3]GalNAc β [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,
15 |
16 NeuNAc α [2 \rightarrow 3]
17 Gal β [1 \rightarrow 3]GalNAc β [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,
18 GalNAc β [1 \rightarrow 4]Gal,
19 GalNAc,
20 Gal,
21 NeuGc \rightarrow GM₃, and
22 NeuNAc \rightarrow GM₃.

1 74. The pharmaceutical preparation as in claim 67, wherein one or more
2 exogenous nucleotide sugar precursor synthesising enzymes are also expressed by said

3 organism, said sugar precursor enzymes forming precursors to make up said chimeric
4 carbohydrate.

SUB AS
1 75. The pharmaceutical preparation as in claim 67, wherein genes encoding
2 the all or some of the one or more glycosyl transferases are modified to prevent phase
3 variation.

1 76. The pharmaceutical preparation as in claim 67, wherein the delivery
2 microorganism is non harmful and live.

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1 77. The pharmaceutical preparation as in claim 67, wherein the delivery
2 microorganism is protected by a protective capsule or held within a protective matrix.

1 78. The pharmaceutical preparation as in claim 67, wherein the target
2 mucosal surface is gastrointestinal.

1 79. The pharmaceutical preparation as in claim 78, wherein the delivery
2 microorganism is selected to provide some resistance to antimicrobial activity of microflora
3 potentially resident in the gut.

SUB AS
1 80. The pharmaceutical preparation as in claim 79, wherein the delivery
2 microorganism is resistant to the major families of colicins.

1 81. The pharmaceutical preparation as in claim 79, wherein the delivery
2 microorganism is grown under conditions to induce acid tolerance.

SUB CS
1 82. The pharmaceutical preparation as in claim 78, wherein the delivery
2 microorganism is enteric.

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1 83. The pharmaceutical preparation as in claim 82, wherein the delivery
2 microorganism belongs to an enteric genera selected from the group consisting of
3 *Escherichia*, *Salmonella*, *Acidophilus*, *Lactobacillus*, *Lactococcus*, *Streptococcus* and
4 *Bifidobacterium*.

1 **84.** The pharmaceutical preparation as in claim 67, wherein the delivery
2 microorganism is killed.

1 **85.** The pharmaceutical preparation as in claim 84, wherein the delivery
2 microorganism is killed by treatment with a chemical agent selected from the group consisting
3 of formalin or thiomersal, or by treatment with a bactericidal antibiotic, or by exposure to
4 heat or UV irradiation.

1 **86.** The pharmaceutical preparation as in claim 67, wherein the carbohydrate
2 molecule is lipopolysaccharide and the carbohydrate is delivered as an intact or partially intact
3 membrane preparation selected from the group consisting of bacterial ghosts, liposomes
4 incorporating chimeric lipopolysaccharide or membrane vesicles.

1 **87.** The pharmaceutical preparation as in claim 67, wherein the carbohydrate
2 is the carbohydrate portion of lipopolysaccharide, and the preparation includes purified or
3 semipurified lipopolysaccharide.

1 **88.** A method of administering a receptor mimic to a mucosal surface of a
2 mammal, the method comprising the administration of a quantity of a delivery microorganism,
3 or parts thereof, the delivery microorganism exhibiting one or more sugars in a configuration
4 to form an exposed receptor mimic, the receptor mimic being a mimic of a receptor of a
5 pathogen, said quantity being sufficient to reduce adherence of the pathogen or a toxin
6 produced by the pathogen to the mucosal surface.

1 **89.** The method of administering a receptor mimic as in claim 88, wherein
2 the delivery microorganism is a recombinant microorganism expressing one or more
3 exogenous sugar transferases and an acceptor molecule, said one or more exogenous sugar
4 transferases being specific for transfer of one or more sugar residues represented
5 progressively from a non reducing terminal end of a receptor of either a toxin or an adhesin of
6 a pathogenic organism, the exogenous sugar transferases progressively transferring said one
7 or more sugar residues onto the acceptor molecule to thereby form a chimeric carbohydrate

18 GalNAc β [1 \rightarrow 4]Gal,
19 GalNAc,
20 Gal,
21 NeuGc \rightarrow GM₃, and
22 NeuNAc \rightarrow GM₃.

1 95. The method of administering a receptor mimic as in claim 88, wherein
2 the receptor mimic of the purified carbohydrate is partially or wholly formed within a sugar
3 moiety selected from the group comprising

4 Gal α [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,
5 GalNAc β [1 \rightarrow 3]Gal α [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc, and
6 Gal β [1 \rightarrow 3]GalNAc β [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc.

1 96. The method of administering a receptor mimic as in claim 95, wherein
2 genes encoding the all or some of the one or more glycosyl transferases are modified to
3 stabilise phase variation.

1 97. The method of administering a receptor mimic as in claim 88, wherein
2 one or more exogenous nucleotide sugar precursor synthesising enzymes are also expressed
3 by said organism, said sugar precursor enzymes forming precursors to make up said chimeric
4 carbohydrate.

1 98. The method of administering a receptor mimic as in claim 88, wherein
2 the delivery microorganism is non harmful and live.

1 99. The method of administering a receptor mimic as in claim 88, wherein
2 the administration is enterally.

1 100. The method of administering a receptor mimic as in claim 99, wherein
2 the delivery microorganism is protected by a protective capsule or held within a protective
3 matrix.

1 **101.** The method of administering a receptor mimic as in claim 99, wherein
2 the delivery microorganism is selected to provide some resistance to antimicrobial activity of
3 microflora potentially resident in the gut.

1 **102.** The method of administering a receptor mimic as in claim 99, wherein
2 the delivery microorganism is resistant to the major families of colicins.

1 **103.** The method of administering a receptor mimic as in claim 99, wherein
2 the delivery microorganism is grown under conditions to induce acid tolerance.

1 **104.** The method of administering a receptor mimic as in claim 99, wherein
2 the delivery microorganism is enteric.

1 **105.** The method of administering a receptor mimic as in claim 104, wherein
2 the delivery microorganism is belongs to an enteric genera selected from the group consisting
3 of Escherichia, Salmonella, Acidophilus, Lactobacillus, Lactococcus and Bifidobacterium.

1 **106.** The method of administering a receptor mimic as in claim 88, wherein
2 the delivery microorganism is killed.

1 **107.** The method of administering a receptor mimic as in claim 106, wherein
2 the delivery microorganism is killed by treatment with a chemical agent selected from the
3 group consisting of formalin, or thiomersal, or a bactericidal antibiotic, or by exposure to heat
4 or to UV irradiation.

1 **108.** The method of administering a receptor mimic as in claim 88, wherein
2 the carbohydrate molecule is lipopolysaccharide and the carbohydrate is delivered as an intact
3 or partially intact membrane preparation selected from the group consisting of bacterial
4 ghosts, liposomes incorporating chimeric lipopolysaccharide or membrane vesicles.

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109. The method of administering a receptor mimic as in claim 88, wherein the carbohydrate is the carbohydrate portion of lipopolysaccharide and the preparation includes purified or semipurified lipopolysaccharide.

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110. The method of administering a receptor mimic as in claim 88, wherein the receptor mimic is that of a porcine rotavirus or shiga like toxin active in pigs, including the step of adding the delivery microorganism to pig feed or drink.

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111. A purified chimeric carbohydrate purified from the recombinant organism of claim 1.

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112. A method of testing for the presence of a toxin or a pathogenic microorganism in a sample, the method comprising:
contacting a sample with the purified carbohydrate of claim 89, either the purified carbohydrate or the sample being immobilized;
washing off unbound purified carbohydrate or toxin or pathogenic microorganism; and
adding detection means to detect bound purified carbohydrate and the toxin or pathogenic microorganism.

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113. The method of testing as in claim 112, wherein the purified carbohydrate is immobilised on a support.

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114. The method of testing as in claim 113, wherein the purified carbohydrate is lipopolysaccharide.

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115. The method of testing as in claim 112, wherein the receptor mimic of the purified carbohydrate is partially or wholly formed within a sugar moiety selected from the group comprising

Gal α [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,

Gal α [1 \rightarrow 4]Gal β ,

GalNAc β [1 \rightarrow 3]Gal α [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,

- 7 Gal β [1 \rightarrow 4]GlcNAc,
- 8 Gal α [1 \rightarrow 3]Gal β [1 \rightarrow 4]Glc,
- 9 Gal α [1 \rightarrow 3]Gal β [1 \rightarrow 4]GlcNAc,
- 10 Gal β [1 \rightarrow 4]GlcNAc β [1 \rightarrow 3]Gal β [1 \rightarrow 4]Glc,
- 11 Glc α [1 \rightarrow 6]Glc,
- 12 Glc α [1 \rightarrow 6]Glc α [1 \rightarrow 6]Glc,
- 13 NeuNAc,
- 14 Gal β [1 \rightarrow 3]GalNAc β [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,
- 15 |
- 16 NeuNAc α [2 \rightarrow 3]
- 17 Gal β [1 \rightarrow 3]GalNAc β [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,
- 18 GalNAc β [1 \rightarrow 4]Gal,
- 19 GalNAc,
- 20 Gal,
- 21 NeuGc \rightarrow GM₃, and
- 22 NeuNAc \rightarrow GM₃.

116. The method of testing as in claim 115, wherein the receptor mimic of the purified carbohydrate is partially or wholly formed within a sugar moiety selected from the group comprising

- 4 Gal α [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc,
- 5 GalNAc β [1 \rightarrow 3]Gal α [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc; and
- 6 Gal β [1 \rightarrow 3]GalNAc β [1 \rightarrow 4]Gal β [1 \rightarrow 4]Glc.